In re Application of:

Sundararajan, et al.

PATENT
ATTY. DOCKET NO.: INTEL1480-2 (P13833X)

Application No.: 10/705,389 Filed: November 10, 2003

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AMENDMENT

Amendments to the Specification:

Following the abstract, please insert the attached Sequence Listing with subsequent page numbering thereafter.

Please replace paragraph [0106] with the following amended paragraph:

FIG. 5 to FIG. 10 illustrates an exemplary method for covering a surface with a [0106] template such as covering a cantilever with an oligonucleotide template. FIG. 5 illustrates the use of a thiol-modified oligo (SH-1-f) [ThiSS] ACAACAACCATCGCCC-TAMRA) (SEQ ID NO:1) that may be bound to a coated surface for example a metal such as a gold thin film layered on a cantilever. TAMRA 501 is just one example of a fluorescent tag that may be attached to an oligonucleotide for detection. The distribution of the thiol-modified oligo may be determined prior to the use of the template for example for sequencing a DNA molecule. The gold substrate may be prepared by using a metallic sputterer at SNF (Ti 50A, Au 1000A on silicon). FIG.6 illustrates one method for determining the surface coverage by a molecule using a bulky group modified template molecule (eg.TAMRA modified oligonucleotide, 16-mer 05). The surface 601 represents a gold-coated surface (eg. cantilever). Then a template such as an oligo with a bulky group (eg. TAMRA 501) may be attached to the coated surface. The bulky group (eg. TAMRA 501, a fluorescent dye that can be incorporated at the end of the DNA strands) 602 is displaced for example by a hydroxide using for example β-mercaptoethanol 603 in a buffer solution and then the film may be removed 604 and the fluorescence measured by a fluorescent spectrophotometer (FIG. 6). In FIG. 7, the fluorescence of the released molecules of a modified surface may be measured at several concentrations and as illustrated here at different dilutions. The concentration of molecules per surface area can be determined using a calibration curve as in FIG. 8 using known fluorescent molecule concentrations. TAMRA is just one example of a fluorescent tag. A number of fluorescent labels are available that can be used for labeling both DNA strands and other biomolecules such as proteins and peptides.

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Please replace paragraph [0111] with the following amended paragraph:

[0111] FIG. 9 illustrates a procedure for finding the hybridization efficiency of a target oligo (SEQ ID NO:2) when it binds to the probe oligo (SEQ ID NO:1). A surface 901 may be functionalized with an oligo probe 902. The functionalized surface may then be hybridized with fluorescently labeled target molecules such as DNA 903. The non-hybridized molecules may then be washed away 904. The remaining double-stranded molecule may then be treated with a denaturant such as sodium hydroxide at basic pH to release the fluorescent-labelled molecule for detection 905. This would indicate the hybridization efficiency of a target molecule.